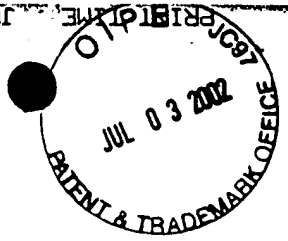

PATENT
ATTORNEY DOCKET NO. UCSD1140-1

#9
JRP
7/23/02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Robert K. Naviaux	Art Unit:	To be assigned
Serial No.:	09/889,251	Examiner	To be assigned
Filed:	July 13, 2001		
Title:	METHODS OF TREATMENT OF MITOCHONDRIAL DISORDERS		

Commissioner for Patents
Washington, D.C. 20231

DECLARATION BY ROBERT K. NAVIAUX

I, Robert K. Naviaux, M.D., Ph.D., declare and state as follows:

1. I am a medical doctor and researcher employed by the University of California, San Diego ("UCSD") School of Medicine. In 1994, following a post-doctoral fellowship at the Salk Institute in San Diego, I became a fellow in human biochemical genetics at UCSD. I joined the UCSD faculty in 1997.

2. At UCSD, I founded and co-direct the Mitochondrial and Metabolic Disease Center and co-founded and serve as the Program Chair of the Mitochondrial Medicine Society. I also serve on the Scientific Advisory Board of the United Mitochondrial Disease Foundation, and I am Associate Editor of the scientific journal *Mitochondrion*. I have published articles and have won several awards for work involving the diagnosis and treatment of mitochondrial diseases and basic mitochondrial biology.

3. On or about June 30, 1995, while I was a research fellow at UCSD, I conceived of a new method of treating patients suffering from mitochondrial disease using pyrimidines such as uridine and triacetyluridine. This invention is described in detail in my published international patent application (PCT No. WO 00/50043).

4. Triacetyluridine is an acetylated prodrug of uridine. Triacetyluridine is available from several chemical supply houses. Pro-Neuron, Inc. ("Pro-Neuron") and its employee and officer Dr. Reid von Borstel have historically tested triacetyluridine for the purpose of reducing the toxicity of certain chemotherapy drugs.

5. I believed my invention would benefit one of my patients, a young child referred to as "CMZ," and I began an experimental course of treatment using uridine on or about July 15, 1996. The treatment was effective. CMZ had regularly suffered seizures and acute sinusitis, as well as serious delays in language, cognitive and motor development. Shortly after treatment began, CMZ exhibited remarkable improvements in these conditions.

6. After my early success in treating CMZ with uridine, I believed that another one of my patients, a 29-year old woman (referred to herein as "KL") would also benefit from the pyrimidine therapy. In early-1998 her condition was deteriorating and no treatment that her doctors had tried had been effective. I had recently been informed that uridine was coming in short supply and I resolved to obtain triacetyluridine for both KL and CMZ.

7. It had not been necessary for me to seek Food and Drug Administration ("FDA") approval to administer ordinary uridine to my patients because it is a naturally-occurring compound. But, in order to use triacetyluridine for experimental medical purposes, I was required to seek approval by the UCSD Institutional Review Board (IRB) and the FDA.

8. On or about January 30, 1998, I contacted Dr. Reid von Borstel at Pro-Neuron to request a supply of triacetyluridine for my patients. I obtained a compassionate use Investigational New Drug Application ("IND") for my CMZ and KL in early February 1998.

9. I began treating CMZ and KL with triacetyluridine in or about February of 1998. A few months later, I obtained FDA approval for a third compassionate use IND to treat an 11-year old boy ("SF"), and I began this treatment on or about April 3, 1998. And I began treating a fourth patient, an infant named "CS" on or about June 19, 1998. I later applied for and was granted and Investigational New Drug approval (IND#56,520) by the FDA to study additional patients.

10. I had a number of other contacts with Pro-Neuron and Dr. von Borstel during 1998 and thereafter. Throughout this time, I provided Pro-Neuron with information and refinements regarding my invention and ongoing reports regarding my clinical results.

11. I understand, on information and belief, that Dr. von Borstel filed a U.S. patent application, No. 09/144,096 on August 31, 1998. This U.S. application to international Patent Cooperation Treaty ("PCT") patent application number WO 00/11952, which was filed on August 31, 1999, and which was published on March 9, 2000. It also led to at least three U.S. applications that have been published: US2001/0005719 (June 28, 2001); US2001/0016576 (Aug. 23, 2001); and US2002/0049182 (April 25, 2002).

12. I have reviewed Dr. von Borstel's published PCT and the three US applications identified above, and I find that the specifications include a significant amount of material similar to my confidential letters and reports to Pro-Neuron. The first four of the examples of each of these applications are the very studies I conducted and reported to Dr. von Borstel. His example number one is the patient "KL"; number two is the patient "SF"; number 3 is the patient "CS"; and number 4 is "CMZ."

13. I declare under penalty of perjury under the laws of the State of California and United States that the foregoing is true and correct. Executed this 27 day of June, 2002 in San Diego, California.

R.K. Naviaux

Robert K. Naviaux, M.D., Ph.D.